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Finnegan, Henderson, Farabow
Garrett & Dunner, L.L.p
1300 I Street, N.W.
Washington, DC 20005-3315

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/225,233
Filing Date: January 04, 1999
Appellant(s): CAMPBELL ET AL.

Salvatore Arrigo
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 16, 2006 appealing from the Office action mailed August 17, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner, which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

An Appeal filed in U.S. Application Serial No. 09/658,862. The Examiner's Answer for '862 is being written concurrent with the present Examiner's Answer.

Appeal to the U.S. District Court for the District of Columbia of the decision from the Patent Board of Appeals and Interferences in I-104,746 and I-105,192 as case numbers 1:05-cv-00353-RMU and 1:05-cv-00706-RMU.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct. However, upon reconsideration, the rejection of claims 147-150 and 156-159 under 35 U.S.C. § 112, first paragraph is withdrawn.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

Grounds of Rejection Withdrawn

The Obviousness-Type Double Patenting rejection made in the office action mailed August 17, 2005 over U.S. Patents 6,147,276, 6,252,133 and 6,525,243 is overcome in view of proper terminal diclaimers filed by appellant on March 31, 2006.

The rejection of claims 147-150 and 156-159 under 35 U.S.C. § 112, first paragraph is withdrawn in view of appellant's comments.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Chense et al. Cloned Rabbits Produced by Nuclear Transfer from Adult Somatic Cells. Nature Biotechnology. April 2002, Volume 20, pp. 366-369.

Galli et al. A Cloned Horse Born to Its Dam Twin. Nature. 07 August 2003, Vol. 424, pp. 635.

Fitchev et al. Nuclear Transfer in the Rat: Potential Access to the Germline. Transplantation Proceed. 1999, Vol. 31, pp. 1525-1530.

Galli et al. A Cloned Horse Born to Its Dam Twin. Nature. 07 August 2003, Vol. 424, pp. 635.

Wakayama et al. Full-Term Development of Mice from Enucleated Oocytes Injected with Cumulus Cell Nuclei. Nature. July, 23, 1998, Vol. 394, pp. 369-374.

Sims et al. Production of Calves by Transfer of Nuclei from Cultured Inner Cell Mass Cells. June 1993, Vol. 90, pp. 6143-6147.

McLaughlin et al. In Vitro Embryo Culture in the Production of Identical Merino Lambs by Nuclear Transplantation. Reproduction Fertility Development. 1990,. Vol. 2, pp. 619-622.

Prather et al. Nuclear Transplantation in Early Pig Embryos. Biology Reproduction. Vol. 41, No. 3, pp. 414-418.

Yong et al. Nuclear Transplantation in Goats. Theriogenology. January 1991, Vol. 35, No. 1, pp. 299.

Cheong et al. Birth of Mice After Transplantation of Early Cell-Cycle Stage Embryonic Nuclei into Enucleated Oocytes. Biology of Reproduction. 1992, Vol. 48, ppl. 958-963.

Yang et al. Nuclear Totipotency of Cultured Rabbit Morulae to Support Full-Term Development Following Nuclear Transfer. Biology of Reproduction. 1992, Vol. 47, pp. 636-643.

Lawrence et al. Feeding Status Affects Glucose Metabolism in Exercising Horses. The Journal of Nutrition. Dec. 1993, Vol. 123, No. 1, 2152-2157.

Gonzales-Pacheco et al. Energy Restriction Reduces Metabolic Rates in Adult Male Fisher-344 Rats. The Journal of Nutrition. January 1993, Vol. 123, No. 1, 90-97.

Zhou et al. Generation of Fertile Cloned Rats by Regulating Oocyte Activation. Science. 14 November 1998, Vol. 302, pp. 1179.

Westhusin, M. E.. et al. Cloning to Reproduce Desired Genotypes. Theriogenology. 2001, Vol. 55, pp. 35-49.

Polejaeva, I. A. et al. Cloned Pigs Produced by Nuclear Transfer from Adult Somatic Cells. Nature. 07 September 2000, Vol. 407, pp. 86-90.

Pennisi and Vogel. Clones: A Hard Act to Follow. Science. 09 June 2000, Vol. 288, pp. 1722-1727.

Wilmut et al. Viable Offspring Derived From Fetal and Adult Mammalian Cells. Nature. 27 February 1997, Vol. 385, pp. 810-813.

Evans et al. Mitochondrial DNA Genotypes in Nuclear Transfer-Derived Cloned Sheep. Nature Genetics. September 199, Vol. 23, pp. 90-93.

Choi et al. In Vitro Development of Equine Nuclear Transfer Embryos: Effects of Oocyte Maturation Media and Amino Acid Composition During Embryo Culture. Zygote. 2003, Vol. 11, 78-86.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states, "whoever invents or discovers any new and useful process ... may obtain a patent therefor..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope.

The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 146-163 remain provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 152-171 of copending Application No. 09/658,862 for reasons set forth in the office action mailed August 11, 2005. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. There is no distinction between the presently claimed nonhuman mammals and those of claims 152-171 in '862. There are no differences between the mammals that renders them distinct in anyway. The only distinction is through their production by separate methods of nuclear transfer (cloning). However, the particular method of nuclear transfer used does not affect the structure, function or use of the claimed nonhuman mammals. Thus, the mammals claimed are the same.

35 U.S.C. § 101

35 U.S.C. 101 reads as follows :

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 146-163 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter for reasons set forth in the office action mailed August 11, 2005. Claims 146-163 are directed to a live born clone of a pre-existing, non-embryonic, non-foetal, donor mammal from which a differentiated cell has been taken, wherein the mammal is selected from cattle, sheep, pigs, goats, mice, rabbits, horses and rats, and where the mammals are produced by nuclear transfer. Claims 146-154 are written as product by process claims where the process is defined in the claims. Claim 155-163 do not contain the particulars of the process steps, but the claims are inherent product by

process claims. Use of the term "clone" to define the mammal implies a method of nuclear transfer, even though the particular steps are not defined.

The claimed mammals do not sufficiently distinguish over pre-existing cattle, sheep, pigs, goats, mice and rabbits. Neither the claims nor the specification point out any characteristics of the claimed mammals that separate them from the pre-existing mammal. The method of making the mammals does not imbue any new or novel characteristic to the cloned mammals nor does the method imbue a new use to the mammals claimed. Further, the claims clearly state that the clone is a copy of a pre-existing mammal. The only discernable difference between the clone and cattle, sheep, pig, goat, mouse, rabbit, horse or rat known in the art at the time of filing is how they were made. The products are each indistinguishable from the previously known product. Hence, the cattle, sheep, pigs, goats, mice and rabbits claimed are not indistinguishable from the cattle, sheep, pigs, goats, mice and rabbits found in nature. Thus, the cloned nonhuman mammals of the claims is not seen as being "new" as required by 35 U.S.C. § 101.

35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 146, 151-155 and 160-163 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for clones of preexisting cattle, sheep, pigs and goats, does not reasonably provide enablement for clones of pre-existing mice, rabbits, horses and rats for reasons set forth in the office action mailed August 11, 2005. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At the time of filing, the skilled artisan would have regarded the cloning of mice, rabbits, horses and rats to be unpredictable. Each having used method steps not taught by the present specification.

Nature of the Invention

The invention is the reproduction of pre-existing non-embryonic, nonhuman mammals by nuclear transfer, or cloning. Nuclear transfer methods require the insertion of a somatic cell or the nucleus of a somatic cell, referred to as the donor nucleus, into an enucleated oocyte, referred to as the recipient cell. If the recipient cell has not been activated prior to the insertion, the cell is activated post-insertion. The enucleated oocyte containing the donor nucleus is referred to as a reconstituted embryo. Although, the methods can vary, the reconstituted embryo is permitted to develop in vitro to the blastocyst stage, and the blastocyst is transferred to the uterus of a surrogate female of the same species as the donor nucleus and recipient oocyte for term development. Dolly, the first mammal cloned by nuclear transfer, is the most famous of mammalian clones. Dolly was produced by insertion of a nucleus of a sheep mammary gland epithelial cell into a sheep enucleated oocyte. As stated by appellant, 277 reconstructed embryos were produced, but only one developed to produce Dolly (Brief, page 12, parag. 4, lines 2-3).

State of the Art at the Time of Filing

At the time of filing, the skilled artisan would have regarded the cloning of mice, rabbits, horses and rats to be unpredictable. Each used method steps not taught by the present specification.

Nuclear transfer in rabbits was successful only when surrogate females were asynchronous by 22 hours from recipient oocytes (Chesne, page 366, col. 1, parag. 1, lines

10-13 and page 367, col. 2, parag. 1). In reporting the birth of a cloned horse, Galli states that the success was aided by advances in assisted reproduction in the horse, including oocyte activation, when both protein synthesis and protein phosphorylation must be inhibited and zona-free manipulation (Galli, page 635, col. 2, parag. 1, lines 7-13). Fitchev states that reconstituted rat embryos were transferred to the uterus of surrogate mothers but none developed to term (Fitchev, page 1528, col. 1, parag. 1, lines 1-3). The problem with rat somatic cell nuclear transfer is due to the spontaneous activation of rat oocytes within 30 minutes of their removal from the oviduct (Zhou, page 1179, col. 1, parag. 2, lines 5-10). Even when a "speedy" enucleation and transfer method was developed, no clones were born (Zhou, col. 2, lines 3-6 and parag. 1, lines 4-7). Successful cloning was reached when MG132, a protease inhibitor that reversibly blocks the first meiotic metaphase-anaphase transition in rat (Zhou, col. 2, parag. 2, lines 10-13). The method used in cloning mice included a prolonged interval between nuclear injection and oocyte activation, suppressing cytokinesis (Wakayama, page 373, lines 1-4). Each method for cloning rabbits, horses, rats and mice used steps materially different and separate from that disclosed in the specification. As the specification does not provide any guidance to the cloning of these species per se, and the ultimate methods were so different, the skilled artisan at the time of filing could not have relied upon the present specification to clone rabbits, horses, rats or mice. Thus, the skilled artisan would have needed to conduct an undue amount of experimentation without a predictable degree of success to implement the claimed invention for its entire breadth.

Guidance and Working Example

The specification teaches a method of nuclear transfer, where the donor cell is quiescent or G0 stage of the cell cycle (specification, page 4, lines 27-30). The specification discloses the method would be useful in the cloning of mammals in general, and specifically

discloses cattle, sheep, pig, goat, mouse, rabbit, horse and rat (specification, page 5, lines 3-24) The specification specifically teaches the production of sheep by nuclear transfer using a quiescent cell as the nuclear donor (specification, pages 32-34). Sheep were produced using adult Fin-Dorset mammary gland epithelial cells, fetal Black Welsh fibroblast or a Pol-Dorset sheep embryonic cell (specification, page 32, lines 1-20). Prior to nuclear transfer, each cell line was made quiescent by culture in media comprising 0.5% serum, an art definition of serum starvation (specification, page 32, lines 31-34). (Note that Dolly resulted from the Fin-Dorset mammary gland epithelial cells that is Dolly was a Fin-Dorset sheep.) The statistics for the production of sheep are given in Tables 2-5 (specification, pages 30, 31 and 34). However, in view of the guidance in the specification and the art at the time of filing, it would have been unpredictable to clone by nuclear transfer the specifically claimed species of mice, rabbits, horses and rats. The specification at the time of filing, and in view of teachings in the art at that time, provide evidence that sufficient guidance was available for the cloning of the specific species cattle, sheep, pig and goat.

35 U.S.C. § 102/35 U.S.C. § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been

> obvious at the time the invention was made to a person having ordinary skills in the art to which said subject matter pertains. patentability shall not be negatived by the manner in which the invention was made.

Claims 146, 147, 155 and 157 (cattle) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sims et al. (1993) Proceed. Natl. Acad. Sci. 90, 6143-6147 for reasons set forth in the office action mailed August 11, 2005.

Sims teaches cloned bovines (page 6146, col. 1, parag. 2, lines 6-11). As the presently claimed cloned cattle do not exhibit a novel structural or functional difference from those described in Sims, Sims anticipates the claimed invention. In the alternative, the claimed cattle is obvious over Sims because there is no perceived structural or functional difference between the claimed cattle and the bovines of Sims. Thus, Sims either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 146, 148, 155 and 157 (sheep) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McLaughlin et al (1990) Reproduction Fertil. Develop. 2, 619-622 for reasons set forth in the office action mailed August 11, 2005.

McLaughlin teaches cloned sheep (page 620, parag. 2-5, and page 621, parag. 1). As the presently claimed cloned sheep do not exhibit a novel structural or functional difference from those described in McLaughlin, McLaughlin anticipates the claimed invention.

In the alternative, the claimed sheep is obvious over McLaughlin because there is no perceived structural or functional difference between the claimed sheep and the sheep of McLaughlin. Thus, McLaughlin either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 146, 149, 155 and 158 (pigs) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Prather et al (1989) Biology of Reproduction 41, 414-418 for reasons set forth in the office action mailed August 11, 2005.

Prather teaches a cloned pig (page 415, col.1, parag. 1 to page 416, line 8, and page 416, col. 2, lines 8-10). As the presently claimed cloned pigs do not exhibit a novel structural or functional difference from the pig described in Prather, Prather anticipates the claimed invention. In the alternative, the claimed pig is obvious over Prather because there is no perceived structural or functional difference between the claimed pigs and the pig of Prather. Thus, Prather either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660,

169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 146, 150, 155 and 159 (goats) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yong et al (1991) Theriogenology 35, page 299 for reasons set forth in the office action mailed August 11, 2005.

Yong teaches cloned goats by nuclear transfer of the reconstituted goat embryos (parag. 2 and Table). As the presently claimed cloned goat does not exhibit a novel structural or functional difference from the goat described in Yong, Yong anticipates the claimed invention. In the alternative, the claimed goat is obvious over Yong because there is no perceived structural or functional difference between the claimed goat and the goat of Yong. Thus, Yong either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 146. 151, 155 and 160 (mouse) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Cheong et al (1993) Biology of Reproduct. 48, 958-963 for reasons set forth in the office action mailed August 11, 2005.

Cheong teaches cloned mice (page 959, col. 1, parag. 2 to col. 2, line 10 and page 962, Table 4). As the presently claimed cloned mouse does not exhibit a novel structural or functional difference from those described in Cheong, Cheong anticipates the claimed

invention. In the alternative, the claimed mice are obvious over Cheong because there is no perceived structural or functional difference between the claimed mouse and the mice of Cheong. Thus, Cheong either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 146, 152, 155 and 161 (rabbits) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yang et al (1992) Biology of Reproduct. 47, 636-643 for reasons set forth in the office action mailed August 11, 2005.

Yang teaches cloned rabbits (page 640, col. 2, parags. 1 and 2, and page 642, Table 4). As the presently claimed cloned rabbit does not exhibit a novel structural or functional difference from those described in Yang, Yang anticipates the claimed invention. In the alternative, the claimed rabbit is are obvious over Yang because there is no perceived structural or functional difference between the claimed rabbit and the rabbits of Yang. Thus, Yang either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660,

169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 146, 153, 155 and 162 (horses) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lawrence et al (1993) The Journal of Nutrition 123, pp. 2152-2157 for reasons set forth in the office action mailed August 11, 2005.

Lawrence teaches standardbred mares and standardbred gelding (page 2153, col. 1, parag. 1, lines 1-4). As the presently claimed cloned horse does not exhibit a novel structural or functional differences from those described in Lawrence, Lawrence anticipates the claimed invention. In the alternative, the claimed horse is obvious over Lawrence because there is no perceived structural or functional difference between the horses. Thus, Lawrence either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 146, 154, 155 and 163 (rats) remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gonzales-Pacheco et al (1993) The Journal of Nutrition 123, 90-97 for reasons set forth in the office actions mailed August 11, 2005.

Gonzales-Pacheco teaches male Fisher 34/NHsd and Harlan Sprague Dawley rats (page 91, col. 1, parag. 2, lines 1-3). As the presently claimed cloned rat does not exhibit a novel structural or functional differences from those described in Gonzales-Pacheco,

Gonzales-Pacheco anticipates the claimed invention. In the alternative, the claimed horse is obvious over Gonzales-Pancheo because there is no perceived structural or functional difference between the rats. Thus, Gonzales-Pacheco either anticipates or makes obvious the claimed invention.

(10) Response to Argument

Statutory Double Patenting

Appellant argues present claims 146-163 recite that the pre-existing mammal is a "non-foetal" mammal, whereas claims 152-171 in copending application serial no. 09/658,862 do not contain this limitation. Thus, appellant argues, identical subject matter is not being claimed. (Brief, page 6, lines 1-4.) These arguments are not persuasive.

Present independent claims 146 and 155 state "a live-born clone of a pre-existing, non-embryonic, non-foetal, donor mammal...". Independent claims 152 and 163 of '862 state "a live-born clone of a pre-existing, non-embryonic, donor mammal ...". While the present claims do indeed, as appellant argues require the donor cell be from a non-foetal mammal, and claims 152 and 163 of '862 do not have this limitation, the donor cell source, be it non-embryonic or fetal, does not distinguish between the products. Once the clone is produced, there is no means to identify the starting material that is the donor cell, be the donor cell non-embryonic or non-foetal. The statutory double patenting rejection is made over the products, which are not provided any distinguishing features by the method of making them. Thus, each set of claims is to patentably indistinct products. The cloned mammals are the same. A cattle (bovine), sheep, pig, goat, mouse, rabbit, horse or rat presently claimed cannot be distinguished from a cattle, sheep, pig, goat, mouse, rabbit, horse or rat claimed in '862. If the products cannot be distinguished, then they are the same invention, even if the method of making the products is not the same invention. If the

products cannot be distinguished, then they are identical. Identical inventions are subject to statutory double patenting. Thus, the rejection made is proper.

35 U.S.C. § 101

Appellant argues that a clone of a pre-existing, non-embryonic, non-foetal, donor mammal is never found in nature (Brief, page 6, parag. 1, line 4). Appellant argues nature never produces progeny by nuclear transfer (Brief, page 6, parag. 2, line 2). Appellant argues nature produces mammalian progeny by sexual reproduction ((Brief, page 6, parag. 2, lines 3-4). Appellant continues that natural sexual reproduction requires a mother and a father, an egg donor and a sperm donor, each with their distinct genetic make-up (Brief, page 7, figure and lines 1-3). Appellant argues the egg and sperm, each with a chromosomal complement, join to create a progeny mammal containing a mixture of the chromosomal complement of the two parents (Brief, page 7, lines 3-6). Appellant argues nature never makes a progeny mammal that is a copy of a single parent (Brief, pages 7-8, bridg. parag.). Appellant argues somatic cell cloning by nuclear transfer results in a progeny mammal that is distinctly different from mammals produced in nature (Brief, page 8, parag. and figure). Appellant explains somatic cell cloning results in a mammal having the same chromosomal complement as a single parent donor mammal (Brief, page 8, parag. 2, lines 1-2). Appellant describes the process of nuclear transfer, and that the donor oocyte does not contribute to the nuclear chromosomal content of the progeny mammal (Brief, page 8-9, bridg. sent.). Appellant argues, in nuclear transfer, the chromosomal complement comes from the nuclear donor mammal, and that the progeny receives its entire chromosomal complement from the donor mammal so the progeny is a genetic copy of the donor mammal (Brief, page 9, lines 2-5).

Appellant argues since nature does not clone mammals by nuclear transfer, the process steps recited in claims 146-154 do not occur in nature (Brief, page 9, parag. 1, lines 1-2). Appellant cites Ex parte Allen 2USPQ2nd 1425, 1426-1427 (Bd. Pat. App. & Int. 1987). Appellant argues the examiner, as the examiner in Allen, has provided no evidence that appellant's claims would exist without the hand of man (Brief, page 9, parag. 1). Appellant argues the Supreme Court in Diamond v Chakrabarty states statutory subject matter includes "anything under the sun that is made by man." *Diamond v. Chakrabarty* 206 USPQ 193, 197 (1980) (Brief, page 9, parag. 2, lines 1-2). Appellant argues their claims require the intervention of man to perform the process step of nuclear transfer in claims 146-154 (Brief, page 10, lines 1-2).

Appellant argues claims 155-163 require a clone of a pre-existing, non-embryonic, non-foetal, donor mammal (Brief, page 10, parag. 1, lines 1-2). Appellant reiterates nature never makes clones of pre-existing, non-embryonic, non-foetal, donor mammals, and thus the clones of claims 155-163 must be made by man (Brief, page 10, parag. 1, lines 3-4). Further, Appellant argues, the examiner has not offered any evidence that appellant's claims would exist without the hand of man (Brief, page 10, parag. 1, lines 4-6). Appellant argues, as recognized by the Supreme Court in Chakrabarty, a non-naturally occurring animal is patentable subject matter under 35 U.S.C. § 101 (Brief, page 10, parag. 2, lines 1-2).

Appellant's arguments are not persuasive.

While appellant has set forth differences in the methods of producing cattle, sheep, pigs, goats, mice, rabbits, horses and rats by sexual reproduction and somatic cell nuclear transfer, appellant does not describe any differences between the resulting products. The issue here is not the method of producing the mammals. Nuclear transfer methods are recognized as having the "hand of man." The issue here is the products of nuclear transfer.

Do the products have the "hand of man." A cattle, sheep, pig, goat, mouse, rabbit, horse or rat produced by somatic cell nuclear transfer is indistinguishable from the same mammal produced sexually. They have the same metabolic and physiologic functions. They have the same uses. Nothing pertaining to the product has changed. While a clone may be produced asexually, the product of the method, it is nonstatutory because it cannot be distinguished from the prior existing mammal (cattle, sheep, pigs, goats, mice, rabbits, horses and rats). There is no discernable difference that lends a patentable distinction between the clone and the pre-existing mammal, although the methods of producing them are different. Claims 146 and 155 clearly state the clone is of a pre-existing mammal. Thus, the claimed mammals are products of nature, just as a mammal produced by IVF would be regarded as a product of nature. Further, the fact that appellant admits the claimed clones are clones of pre-existing mammals is evidence that the mammals exist or existed without the hand of man. Thus, the criteria of Allen, as stated by Appellant, is provided. With regard to the "hand of man" in Chakrabarty, in a side-by-side comparison with the pre-existing mammal, the cloned mammals could not be seen to have any evidence of a "hand of man." Having the same chromosomal complement of the pre-existing mammal lends further credence to the clones being non-statutory (Brief, page 9, lines 3-5). If the clones are the same as what appellant would agree is a product of nature, a mammal produced by sexual reproduction, then the mammals produced by nuclear transfer must also be products of nature. While there is evidence of the hand of man in methods of nuclear transfer, there is no evidence of the hand of man in the presently claimed live-born clones.

35 U.S.C. § 112

Mouse, Claims 151 and 160 (Brief, pages 12-14.)

Appellant argues the examiner's position ignores the low efficiency of the cloning process (Brief, page 11, parag. 1, lines 1-2). Appellant argues the papers cited by the

examiner in the enablement rejection simply show that there may be ways to increase the efficiency of cloning by optimizing appellant's invention (Brief, page 11, parag. 1, lines 2-3). Appellant argues any conclusions regarding the cloning of mammals must take into account the low efficiency of the cloning process (Brief, page 11, parag. 1, lines 3-5). Appellant argues the experimentation needed to achieve successful cloning would be repetitive and therefore routine, as permitted (*In re Wands*, 858 F.2d 731, 737; 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) (Brief, page 11, parag. 1, lines 7-10). Appellant argues there is no evidence of record that one of skill in the art would not succeed in using appellant's method to produce appellant's claimed mammals when the inefficiency of appellant's process is taken into consideration (Brief, page 11, parag. 2, lines 1-3). Appellant argues the Office has not alleged that appellant's claimed process will not work if performed a sufficient number of times (Brief, page 11, parag. 2, lines 3-5). Appellant argues improvements on their method does not negate the enablement of their method. These arguments are not persuasive.

The art at the time of filing does not support appellant's arguments. For example, Westhusin (2001), states that one of the major factors influencing a successful cloning outcome is species of target animal. Westhusin goes on to state that while the basic methodology for nuclear transfer may be similar, the specific materials and methods do not automatically apply across all species. Westhusin outlines six factors which contribute to successful cloning: 1) acquisition of mature ova, 2) removing the chromosomes contained within the ova, 3) transfer of cell nuclei obtained from the animal to be cloned into enucleated ova, 4) activation of the newly formed embryo, 5) embryo culture in vitro, and 6) transfer of the cloned embryo into a surrogate mother. Westhusin further states that each of these steps will vary slightly between species, but that, more importantly, the efficiency of each step varies among species, ultimately affecting the ease of which a

particular animal can be cloned (see Westhusin (2001) Theriogenology 55, page 36-37, bridg. parag.). This analysis is supported by Polejaeva (2000) that states, in regard to the inefficiency of cloning, that several factors affect the inefficiency: laboratory to laboratory variation, oocyte source and quality, methods of embryo culture, donor cell type, possible loss of somatic imprinting in the nuclei of the reconstructed embryo, failure to reprogram the transplanted nucleus adequately, and failure of artificial methods of activation to emulate reproducibly those crucial membrane-mediated events that accompany fertilization (Polejaeva (2000), page 1, parag. 2). Thus, the degree of experimentation does not provide for the predictable success required by the "Wands Factors." Appellant uses the term "inefficiency" to imply that all one has to do is tweak a few experimental factors in nuclear transfer, or to make many reconstructed embryos. However, a fair reading of Westhusin et al and Polejaeva et al indicates that "inefficiency" falls under the heading of "an undue amount of experimentation without a predictable degree of success." Given the teachings of Chesne et al, Galli et al, Fitchev et al, Zhou et al and Wakayama et al, as discuss further below in rebuttal to appellant's arguments, the particularly claimed species of rabbit, horse, rat and mouse fall as indicated by Westhusin et al and Polejaeva et al, as requiring an undue amount of experimentation without a predictable degree of success.

Further, it should also be noted that Pennisi and Vogel cites several scientists working in the area of mammalian cloning who point to a lack of general and reproducible success, thus, emphasizing the lack of predictability at the time of filing. Robert Wall of the USDA is quoted as stating that despite years of effort, "[w]e're in the same bind that we've always been in. A majority of [would be clones] do not make it to term." (Pennisi and Vogel (2000), page 1722, col. 1, parag. 2, lines 9-14). Pennisi and Vogel state that "even when an embryo does successfully implant in the womb, pregnancies often end in miscarriages" (Pennisi and Vogel (2000), page 1722, col. 1, parag. 3, lines 16-18). The case with rabbits

indicates that obtaining an embryo by nuclear transfer does not translate into a cloned rabbit. While many cloned rabbit embryos can be made, they abort upon transfer to surrogate mothers, and in 2000, there had not been any successes in cloning rabbits (Pennisi and Vogel (2000), page 1725, col. 2, parag. 3). As the authors state, establishing pregnancies is only part of the problem and is not a guarantee of a cloned mammal being produced (Pennisi and Vogel (2000), page 1726, col. 2, lines 9-11). Thus, at the time of filing, the art of Pennisi and Vogel provide support that cloning by nuclear transfer for individual species requires species-specific protocols in order to achieve live births. No such protocols are suggested by the specification or the art at the time of filing for rabbit, horse, rat or mouse. Nowhere are the particular protocols of Chesne et al, Galli et al, Fitchev et al, Zhou et al or Wakayama et al suggested in the specification or the art at the time of filing. There was no guidance at the time of filing to lead the skilled artisan to implement these particular protocols for successful cloning of rabbit, horse, rat and mouse.

Appellant argues the sole basis for questioning the enablement of mice is based on a paper reporting successful cloning of mice using somatic cell nuclear transfer, Wakayama et al (Brief, page 12, parag. 3, lines 1-3). Appellant argues the examiner's position does not appreciate the low efficiency of nuclear transfer (Brief, page 12, parag. 4, lines 1-2). Appellant refers to the specification, where only one lamb out of 277 "fused couplets" (Brief, page 12, parag. 4, lines 2-3). Appellant argues enablement does not hinge on how many times a procedure must be repeated to obtain a successful outcome, and that repetition is routine (Brief, page 12, parag. 4, line 5 to page 13, line 2). These arguments are not persuasive.

The specification discloses only one lamb being born from a protocol, where activation and fusion occur simultaneously (specification, page 27, lines 8-11 and Wilmut, page 813, col. 1, parag. 2, lines 1-3). In this procedure, a differentiated cell from a pre-

existing, non-embryonic, non-foetal sheep, in this case a mammary gland epithelial cell (OME for ovine mammary epithelial) from a 6-year old female sheep, was used as nuclear donor (specification, page 32, lines 5-10). Of 277 fused and activated reconstituted embryos only one cloned sheep was produced (specification, page 34, Table 4, see OME). Thus, for the method claimed, where a cell from an "adult" cow, sheep, goat, pig, rabbit, horse, mouse or rat is the nuclear donor, only one sheep was produced. This alone does not speak well for reproducibility, or enablement as reproducibility is an issue for enablement. Further the specification, discloses parallel experiments in cattle. However no results are given. The specification states no transfers of cattle embryos to final recipients were made (specification, page 29, lines 22-25). Thus, there is no evidence that if a sufficient number of reconstructed embryos were produced, a cloned cattle would have been achieved. Appellant's argument, if enough reconstructed embryos are made, eventually, a cloned mammal using the presently claimed method will result, is not supported by evidence. In deciding enablement, the issue is predictability of success without undue experimentation. Given the disclosure, the skilled artisan would need to engage in an undue amount of experimentation, without a prediction of success to achieve the cloning of rabbits, horses, mice and rats. The species for which enablement was given (cattle, sheep, goats and pigs) are mammals that had been cloned by those of skill in the art using methodologies lacking an inventive concept, where any deviations between the successful methodologies and the methodology claimed, obviously lies in the realm of routine experimentation.

Appellant further argues the specification teaches the prolonged interval between nuclear injection and oocyte activation (see specification page 11, lines 28-30) (Brief, page 13, parag. 2, lines 1-3). Appellant argues the examiner concedes the application discloses 6-20 hours for cows and the time is species dependent (see Advisory Action, December 21, 2005) (Brief, page 13, parag. 2, lines 3-4). Thus, appellant argues no undue

experimentation would have been required to arrive at Wakayama's 1-6 hour delay of activation (Brief, page 13, parag. 2, line 11 to page 14, line 2). Further, appellant argues the specification teaches an example using unactivated metaphase II oocytes, where prior to activation, reconstituted embryos were incubated for more than 30 minutes (specification, page 23, lines 28-32) ((Brief, page 14, parag. 1, lines 6-8). Appellant argues although the exact times for oocyte incubation are not given, the specification makes clear an incubation time of more than 30 minutes prior to activation between nuclear injection and oocyte activation (Brief, page 14, parag. 1, lines 8-12).

The central issue is if the specification provides guidance for the time interval between nuclear injection into the enucleated oocyte and oocyte activation specifically used by Wakayama. The specification does not provide any guidance as to the length of time between nuclear injection and activation, although the "Magic" protocol seems to have at least 30-minute incubation (specification, page 11, lines 28-30; page 23, lines 30-32). However, the length of incubation between nuclear transfer and activation, according to Wakayama, is not the only reason for the success in mice. Wakayama notes the use of a piezo-impact pipette driven unit may have lead to the increase in embryonic development to term because oocyte and donor nucleus manipulations were quick and efficient, eliminating trauma to both in comparison to electrofusion, Sendai virus or polyethylene glycol (Wakayama, page 373, col. 1, lines 11-16). Wakayama states the amount of somatic cell cytoplasm introduced into the oocyte was minimized (Wakayama, page 373, col. 1, lines 16-19). Additionally, Wakayama obtained mouse clones only from one cell type, cumulus cells, which are in the G1/G0 phase of the cell cycle (Wakayama, page 370, col. 1, lines 3-5). Sertoli cells and neuronal cells, each naturally in the G0 phase of the cell cycle, did not result in cloned mice (Wakayama, page 370, col. 1, lines 1-2; and page 371, col. 2, parag. 2, lines 4-8 and Table 2). Thus, the evidence is G0 mouse cells will not support nuclear

transfer. The methodology of the present claims, where the cattle, sheep, goats, pigs, mice, rabbits and rats clones are claimed, requires that the animals be made from quiescent cells, that is cells in G0. Thus, Wakayama offers evidence that appellant's method is not enabled for mice, as mice cannot be made using G0 cells. Wakayama's successes were all from cumulus cells, using methodologies that cannot be regarded as routine alterations to the methodology disclosed in the specification. Nothing the specification would lead one to a piezo-impact driven pipette in conjunction with an 1-6 hour incubation between injection of the nucleus into the oocyte and activation. These methodologies are inventive concepts not disclosed or contemplated by the specification. Further, while appellant agrees that there is a 6-20 hour delay for cows, it is noted that the methods disclosed are not reported to be successful with cows.

Rabbits, Claims 152 and 161 (Brief, pages 14-16.)

Appellant argues the examiner's position does not take into account the general low efficiency of the cloning process (Brief, page 15, parag. 1, lines 1-2). Appellant argues there is no evidence of record that one of skill in the art would not succeed in using appellant's method to produce rabbits when the inefficiency of appellant's process is taken into account (Brief, page 15, lines 2-4). Appellant argues the office does not allege that appellant's process will not work if nuclear transfer is performed a sufficient number of times (Brief, page 15, parag. 1, lines 4-6). These arguments are not persuasive, and are the same arguments presented above.

With regard to cloning rabbits as claimed, the art taught rabbit embryos could be produced by nuclear transfer, but they abort upon transfer to surrogate mothers (Pennisi and Vogel (2000), page 1725, col. 2, parag. 3 and Chesne, page 366, col. 1, parag. 10-13). Thus, it was not until Chesne further added asynchronization of reconstituted embryos and recipient female that cloned rabbits were first produced (page 366, col. 2, parag. 1, lines

14-17). Chesne clearly states attempts of cloning rabbits by somatic cell nuclear transfer had been unsuccessful up to their addition of asynchronization (Chesne, page 367, col. 2, parag. 1, lines 1-4). The evidence of Chesne is that without asynchronization, it would not matter how many embryos were made, cloning would not be successful.

Appellant argues ways to improve the efficiency of Appellant's method does not negate that appellant's cloned rabbits are enabled (Brief, page 15, parag. 2, lines 1-2). Appellant argues Landa and Al-Hasani et al provide evidence that asynchronous embryo transfer in rabbits was known in the art at the time of filing (Brief, page 15, parag. 2, lines 2-5). Appellant argues Landa used, with in vitro cultured rabbit embryos, asynchronous embryo transfer to achieve successful production of rabbits (Appeal Brief, page 15, parag. 2, lines 10-12). Appellant concludes Chense's use of Landa's method was not surprising. Appellant argues Al-Hasani compared synchronous and asynchronous embryo transfer with in vitro cultured rabbit embryos (Brief, page 16, parag. 1, lines 1-2). Appellant argues Al-Hasani concluded in vitro culture of rabbit embryos lead to a delay in development and the delay was time in culture dependent (Brief, page 16, parag. 1, lines 2-5). Appellant argues Al-Hasani found the delay could be compensated for by using asynchronous recipient rabbits (Brief, page 16, parag. 1, lines 5-8). Appellant argues the use of asynchronous nuclear transfer was known at the time of the present invention, and that the skilled artisan would have known, for rabbits, to use asynchronous nuclear transfer. These arguments are not persuasive.

Chesne does not improve the efficiency of appellant's method. Improving efficiency implies there was some success. As cited above, Chesne states there were no cloned rabbits produced by nuclear transfer. Thus, Chesne modified appellant's method using a protocol not suggested by appellant, and doing so produced cloned rabbits. Landa applied asynchronous embryo-recipient female transfer in the production of rabbits from embryos

produced by sperm-oocyte fertilization, and not by nuclear transfer. Al-Hasani used embryos produced through in vitro fertilization (Al-Hasani, page 191, parag. 3). There is no teaching in Landa or Al-Hasani that asynchronous transfer would be useful to or should be applied to nuclear transfer methods. Further, the methologies of nuclear transfer, of the present invention, and embryo transfer of Landa or Al-Hasani, are not co-extensive. There was no prediction of successful outcome in applying the teachings of Landa or Al-Hasani to those of appellant, as the degree of manipulation in nuclear transfer is much more extensive. The asynchronous transfer method of Landa and Al-Hasani were well known at the time of filing for embryo transfer, where the embryos were produced either by in situ fertilization or in vitro fertilization. There was no suggestion to use the synchronous method to nuclear transfer embryos.

Horse, Claims 153 and 162 (Brief, pages 17-19.)

Appellant argues the examiner's position does to take into account the general low efficiency of the cloning process (Brief, page 17, parag. 2, lines 1-2). Appellant argues there is no evidence of record that one of skill in the art would not succeed in using appellant's method to produce horses when the inefficiency of appellant's process is taken into account (Brief, page 17, parag. 2, lines 2-4). Appellant argues the office does not allege that appellant's process will not work if nuclear transfer is performed a sufficient number of times (Brief, page 17, parag. 2, lines 4-6). These arguments are not persuasive, and are the same arguments presented above.

Appellant argues the methodologies used by Galli were known prior to appellant's filing date to improve cloning efficiencies (Brief, page 17, parag. 3, lines 2-4). Appellant argues that Galli points to Lazari for the proposition that both protein synthesis and protein phosphorylation must be inhibited (Brief, page 17, parag. 3, lines 4-6). Appellant argues Lazari only discuses activation studies performed on horse oocytes with a known protein

synthesis inhibition or a known protein phosphorylation inhibitor, either alone or in combination, further in association with ionomycin (Brief, page 17, parag. 3, line 7 to page 18, lines 2). Appellant argues Susko-Parrish taught at the time of filing the use CHX and DMAP, as disclosed in Lazari, in oocyte activation at the time of filing (Brief, page 18, parag. 2, lines 2-6). Appellant argues Galli also references Lagutino for the use of zona free horse oocytes, but such is not necessary for creating a horse (Brief, page 18, parag. 2, lines 1-3_. Appellant argues that Lagutino obtained high fusion and cleavage rates even when intact zona oocytes were used (Brief, page 18, parag. 2, lines 4-7). Appellant argues that Lagutino conventional methods of fusion, available at the time of filing, were adequate to clone horses. These arguments are not persuasive.

The evidence in the art is horses could not be cloned using a method very similar to appellant's method where quiescent fibroblasts were used as nuclear donor, although pregnancies were achieved (Choi, page 78, parag. 1-6). Using methods similar to appellants did not yield any nuclear transfer, reconstructed embryos for transfer (Choi, page 78, col. 1, parag. 1, lines 6-22). Choi indicates that conditions for equine nuclear transfer need significant research (Choi, page 78, parag. 2, lines 1-8). Thus, the art supports the examiner's rejection that horses are not enabled by the present specification.

Further, Galli's method employs three method steps not disclosed in the present specification: inhibiting both protein synthesis and phosphorylation during activation, not one or the other as taught by the specification and Susko-Parrish, in addition to zona-free oocytes. It is the combination of these three alterations to appellant's method, and not disclosed in the present specification, that enable the production of horses. When this is taken in view of Choi, above, concerning horse nuclear transfer all attempts at cloning by nuclear transfer, using a method very similar to appellants, failed, the specification fails to

enable the particular species, horse, and the successes in the post-filing art cannot be attributed to appellant's disclosure.

Rats, Claims 154 and 163 (Brief, pages 19-20.)

Appellant argues the examiner's position does to take into account the general low efficiency of the cloning process (Brief, page 19, parag. 3, lines 1-2). Appellant argues there is no evidence of record that one of skill in the art would not succeed in using appellant's method to produce rats when the inefficiency of appellant's process is taken into account (Brief, page 19, parag. 3,lines 4-6). Appellant argues the office does not allege that appellant's process will not work if nuclear transfer is performed a sufficient number of times (Brief, page 19, parag. 3, lines 4-6). These arguments are not persuasive.

Zhou states nuclear transfer (cloning) in rats "all previous attempts to clone rats have been unsuccessful, with developmental arrest at implantation stage" (Zhou, page 1179, col. 1, parag. 1, lines 11-15). Thus, Zhou teaches the cloning of rats was not enabled at the time of the present invention.

Appellant argues that improvements in efficiency through optimization does not negate that appellants cloned rats are enabled (Brief, page 19, parag. 4, lines 1-2). Appellant argues that MG132 reversibly blocks the first meiotic metaphase-anaphase transition, thereby maintaining the oocytes in a non-activated state (Brief, page 19, parag. 4, lines 2-5). Appellant argues that the present specification teaches reconstructing embryos using a non-activated MII arrested oocyte (Brief, page 19, parag. 5, line 6 to page 20, line 2). (Note the reference in the Brief to page 4 is incorrect. Please refer to page 23 of the specification "MAGIC" for MII arrested oocytes.) These arguments are not persuasive.

A methodology is not an "improvement" when the methodology results in cloned rats and methods known in the art beforehand resulted in zero cloned mice. An improvement, in a patentability context, means of the successes known in the art, the new method makes

more or better cloned rats, not that it makes cloned rats when none were made before. This is the issue here. Whatever MG132 does to the rat oocyte, it makes nuclear transfer successful and cloned rats are achieved. Nowhere in the present specification does the use of MG132 or any other chemical that maintains the oocytes in MII suggested. Since Zhou first produced cloned rats and used methodology not disclosed in the specification, the specification cannot be regarded as enabling for this species of mammal.

35 U.S.C. § 102/35 U.S.C. § 103

35 U.S.C. § 102(b)

The main thrust of appellant's arguments is the prior art of record does not disclose animals that have all of the properties of appellant's claimed clones. It is appellant's contention that the cattle (Sims et al.), sheep (McLaughlin et al.), pigs (Prather et al.), goats (Yong et al.), mice (Cheong et al.), rabbits (Yang et al.), horse (Lawrence) and rats (Gonzale-Pacheo) cited by the examiner are not identical to the claimed invention, and thus cannot anticipate the claims (Brief, page 20, parag. 2). Appellant argues a mammal identical to appellant's clone never existed before appellant's invention (Brief, page 20, parag. 3, line 5 to page 21, line 2). This argument is not persuasive.

Claims 146 and 155 each state "a live-born clone of a pre-existing .... mammal." Thus the examiner takes exception to appellant's argument that the mammal of the claims "never existed before." The claim clearly states the clone was made from an animal that pre-existed. Thus, if the clone is copy of a pre-existing mammal, then the clone, a facsimile of the pre-existing mammal, did exist before. It is a copy. The specification states, in describing improvements of somatic cell nuclear transfer over embryonic cell nuclear transfer that cloned offspring are identical to the cultured cell nuclear donor:

The ability to produce cloned offspring from a cultured cell line would offer a large number of advantages over the use of early embryos. These include: the production of ***large***

numbers of identical offspring over a long time period (cultured cells can be frozen and stored) and the ability genetically to modify and/or select cell populations of the required genotype (e.g. sex) prior to embryo reconstruction. (Specification, page 1, lines 26-33).

Thus, the specification clearly states a clone is identical to its nuclear donor. Thus, appellant's claimed mammals are considered by the specification to be identical to the pre-existing mammal, the source of the nucleus in the nuclear transfer method. Therefore, while appellant's method of nuclear transfer or method of cloning by nuclear transfer maybe very well be novel and non-obvious, the resulting mammals are neither novel or non-obvious. The resulting mammals are identical to the donor nucleus. As such, a clone cannot be patentably distinguished from pre-existing cattle, sheep, pig, goat, mouse or rabbits.

1. The specification explains that appellant's clone is not identical to the clone's parent. (Brief, page 21.)

2. The evidence of record demonstrates that appellant's clone is not identical to the clone's parent. (Brief, page 21-23)

Appellant argues that although the specification states the clones are identical, the specification doesn't really mean clones are identical to the nuclear donor mammal or cell because they are derived from different oocytes (Brief, page 21, parag. 2, lines 1-3). Appellant argues the specification states that significance of the difference is not clear, but mitochondrial DNA in diary cattle maybe related to milk and reproductive performance (Brief, page 21, parag. 1, lines 6-10). Appellant argues differences in mitochondrial DNA may contribute to genetic differences between a clone and its parent (Brief, page 22, lines 4-6). Appellant argues evidence has been present during prosecution that the clone is not identical to its parent (Brief, page 21, parag, 3, lines 1-2). Appellant points to teachings in Prather et al (1990), hereafter Prather (2000), which state a clone is not identical to the clone's parent because of spontaneous rearrangements in genes, especially immunoglobulin genes, gene amplifications, translocations, and diminution (Brief, page 21 parag. 3, line 4 to

page 22, lines 4). Appellant additionally points to Prather (2000) teaching and declarant Wells (declaration by David Wells, filed February 10, 2003) stating environmental factors, such as the uterine environment, generate differences that prevent a clone and its parent from being phenotypically identical. Appellant points to a clone and its parent having different coat color due to differences in melanocyte migration (Brief, page 22, parag. 1, lines 3-6). Further, Appellant argues every iris is unique, and clone would have different pigmentation of the iris as compared to its parent, and appellant points to U.S. Patent 4,641,349 for support (Brief, page 22, parag. 1, lines 6-8). Appellant argues a clone that contains the same set of chromosomes as a single parental mammal can be distinguished from the parental mammal due to these environmental influences, as stated by declarant Wells (Brief, page 22, parag. 1, lines 8-11). Appellant states the clone will have behavioral differences from the parental mammal (Brief, page 22, parag. 2). These arguments are not persuasive.

While discussing random genetic and epigenetic differences between a clone and the donor mammal, neither Prather nor declarant Wells correlate gene amplification, translocation, rearrangement or diminution, or an epigenetic phenomenon with any new characteristic of the clone that provides the clone with novelty and nonobvious over the nuclear donor mammal. Two products will rarely be absolutely, positively identical phenotypically. Two "identical cars" may have a variation in paint thickness somewhere, as an example, but they function identically. Likewise, two animals that function identically may have differences in coat color or other phenotypic differences. However, there is no evidence that these random events discussed in the art affect the use of the clone over the nuclear donor. Prather (2000) comments that having genetically uniform animals would be very useful (Prather (2000), page 11, col. 1, parag. 1, lines 13-16). Thus, there is no evidence in Prather (2000) or the Wells declaration of phenotypic differences that may

affect the clone such that it has any patentably distinguishing characteristics over the nuclear donor mammal. To carry appellant's arguments further, a cow with a twisted horn would be novel and nonobvious over a cow with a smooth horn, or a goat with a particular nucleic acid residue at a particular position in its genome would be novel and nonobvious over a goat with a different nucleic acid residue at the same position of its genome, even if there is no alteration between the animals physiology. A cow that functions as a cow, just like a goat that functions like a goat, cannot be separately patentable because of a twisted horn, coat color or nucleic acid sequence unless a novel and nonobvious characteristic arises. In a similar fashion, iris differences between species (US Patent 4,641,349) do not affect the innate use of the animals. While one maybe able to tell one animal from another animal based on iris structure, this characteristic does not provide a novel and nonobvious feature to the animal to make one patentable over the other solely based on iris structure. Further, US Patent 4,641,349 deals with individuals produced sexually. There is no discussion of iris structure in clones. Since body structure is a genetic phenomenon, a clone and the nuclear donor mammal could have the same iris structure. Likewise, a cloned mammal with a mitochondria genotype different from the nuclear donor mammal cannot be patentable over the donor mammal unless the mitochondria genotype provides for a novel and nonobvious characteristic, property or phenotype. While Prather discusses epigenetic phenomenon as potentially altering the phenotype of the clone, Prather never makes the blanket statement that such phenomenon will always occur, "may have a red patch over its eye" (Prather (2000), page 10, col. 2, parag. 4, lines 9-11). It is important to note Appellant's claims do not contain limitations to genetic mutation or epigenetic phenomenon. Thus, the claims encompass cloned nonhuman mammals that have had and have not had such alterations.

It is also important to note, the specification, finds no evidence that appellant contemplated or considered their clones as "different" from the nuclear donor mammal. The only relevant discussion concerns potential mitochondrial differences, pointed to above (specification, page 19, lines 1-9). However, even this difference is not clearly indicated to affect the clones or the use of the clones. The specification states confirmation is needed that effects in milk and reproduction performance are mitochondria related and occur through out the cattle population (specification, page 19, lines 15-18). The specification does not suggest any screening or selection process for choosing oocytes to be used in nuclear transfer. Thus, at the time of filing, appellant showed no consideration that oocytes affected cloning outcome.

Further, the claims encompass a situation where the oocyte and the nucleus are from mammals that have the "same" mitochondria. Evidence has not been presented that every individual of every nonhuman mammal species contains a different mitochondria. As an example, in the production of Dolly, the first mammal cloned by somatic cell nuclear transfer, the nuclear donor in the production of Dolly was a Finn Dorset ewe (Wilmut, page 812, figure 2). The recipient oocyte came from a Scottish Blackface ewe. Dolly had mitochondria of the Scottish Blackface ewe (Evans, page 92, col. 2, parag. 2, lines 1-3). However, if Dolly had been made by putting a Finn Dorset cell nucleus into a Finn Dorset oocyte, the mitochondrial composition of Dolly may have been the "same" as the donor cell. Since the claims and the specification do not limit the claims to mammals produced using recipient oocytes and donor cells of different mitochondrial compositions, the claims encompass the situation were the recipient oocytes and nuclear donor cells are of the same mitochondrial composition so that the clone and the nuclear donor cell have the "same" mitochondrial composition. Since the specification omits any discussion on choosing a recipient oocyte based on mitochondrial genome, it is within the context of the claims for

the recipient oocyte, and thereby the resulting clone, and the donor mammal to have the "same" mitochondria.

Neither Appellant, declarant nor Prather elaborate on any behavioral differences between the clone and the pre-existing mammal. How behavioral differences affect the novelty and nonobviousness of a clone, is not clear.

Appellant argues the cloned mammal will always be of a younger age than the parent mammal since the parental mammal must exist before the clone can exist. Appellant refers to declarant Wells at parag. 35. Appellant argues that the age difference means the clone and the pre-existing mammal cannot be identical. With reference to Dolly Appellant argues, Dolly existed at a later time than her parental donor mammal and Dolly was produced using a cell from a six year old sheep and would never be confused with her mother as they are not identical. These arguments are not persuasive.

Age alone cannot be a determining factor in the patentably of cloned mammals over pre-existing nuclear donor mammals. In a side-by-side comparison of a fourteen-year-old cloned cat and a fifteen year old nuclear donor cat, an age difference would not be discernable. Even in situations where an age difference can be discerned such as a one year old cow and a five-year-old cow, there is nothing novel or nonobvious between the mammals based on age. First off, the five-year-old cow was one year old, albeit four years earlier, so having been one year old is an inherent feature. However, importantly, there is no novel or nonobvious feature, characteristic or phenotype found in the younger animal. The specification does not teach age as an immutable characteristic that imbues patentable distinction. As for Dolly, she was produced by nuclear transfer using a cell from a six-year-old sheep. Had Dolly's nuclear donor parent been around when Dolly was six, there is every likelihood that a six-year-old sheep clone and its twelve-year-old sheep nuclear donor would look identical. This is especially noteworthy given Dolly's telomere age at birth was six,

supposedly. Does this mean at chronologic age six, Dolly was really twelve. If so, she probably was identical in looks to the nuclear donor sheep, barring any scarring. However, all of this is irrelevant, as age is not disclosed in the specification or disclosed in the art as providing a difference between a clone and its pre-existing nuclear donor mammal.

35 U.S.C. § 103 (Brief, pages 23-25.)

Appellant argues clones are set apart from all the animals in the prior art because they are time-delayed copies of pre-existing animals (Brief, page 24, parag. 1, lines 1-2). Appellant argues that only a mammal cloned by somatic cell nuclear transfer will contain the same set of chromosomes as a single parental mammal (Brief, page 24, parag. 1, lines 5-7). Appellant refer to Declarant Wells at parag. 34. Appellant argues since cloning by somatic cell nuclear transfer was thought to be impossible prior to Appellant's invention, this feature of appellant's clones cannot be considered to have been obvious over mammals produced by sexual reproduction (Brief, page 24, parag. 2, lines 9-12). These arguments are not persuasive.

As argued above, the age of the clone versus the age of the nuclear donor mammal does not provide a novel and nonobvious feature to the clone. There is no alteration to the clone based on the method of making it that provides a novel and nonobvious feature to the clone. Being a time-delayed copy does make the clone "younger" but the donor mammal has already been the younger age, making the clone obvious. It is obvious that a ten-year-old mammal was once five years old. This would render a five-year-old clone of the ten-year-old mammal obvious. The method of making the clone is indeed novel and nonobvious, as evidenced by the issuance of several patents to the technology. However, the issue in this case is not the method but the product produced by the method. In particular, the question asked is whether or not the method of making a clone by somatic cell nuclear transfer makes the clone patentable over a pre-existing mammal. Since the method of

nuclear transfer does not provide a novel or nonobvious property to the clone, or provide some other phenotype or use not found in the pre-existing mammal, the clone is not patentably distinct from a pre-existing mammal. In a side-by-side comparison, patentable distinct could not be determined. The specification does not teach this, and appellant has not provided for any. The clone and the pre-existing mammal have the same set of chromosomes, by Appellant's own admission ((Brief, page 24, parag. 1, lines 5-6). Further Declarant Wells states the same thing (Wells Declaration, parag. 34). Thus, the record admits the clone and the pre-existing mammal are the same or obvious over each other. Any phenotypic differences are not seen as providing any degree of patentable distinction. The cloned mammals have same properties, characteristics and uses as the nuclear donor mammals.

Appellant argues the clones are a time delay copy of the pre-existing nuclear donor mammal (Brief, page 25, parag. 1, lines 1-2). Appellant argues the age difference between the clone and pre-existing mammal could not have been expected from the prior art because prior to their invention, a mammal cloned by nuclear transfer. Appellant argues Dolly existed at a time later than the donor sheep, and no one would have contended that doll was obvious in view of her mother. Appellant argues that prior to their invention, the production of such a mammal was not possible. These arguments are not persuasive.

Again, the products are being examined in this prosecution and not methods of nuclear transfer. Dolly the sheep is indeed obvious over her mother. The method of producing Dolly did not give Dolly any novel or nonobvious features over the mother. It isn't the existence of Dolly that is at issue, but Dolly, and her cloned peers. The specification, the art nor declarant Wells have set forth any evidence that a cloned mammal is patentably distinct from the pre-existing nuclear donor mammal

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630

Conferees:

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

Deborah Reynolds

DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600